

## EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	267	GDH and mutant	US-PGPUB; USPAT; DERWENT	OR	ON	2006/06/23 13:12
L2	55833	thr	US-PGPUB; USPAT; DERWENT	OR	ON	2006/06/23 13:12
L3	99	l1 and l2	US-PGPUB; USPAT; DERWENT	OR	ON	2006/06/23 13:12
L4	1	l1 and thr366	US-PGPUB; USPAT; DERWENT	OR	ON	2006/06/23 13:13

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PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS 1            Web Page URLs for STN Seminar Schedule - N. America  
NEWS 2            "Ask CAS" for self-help around the clock  
NEWS 3 JAN 17     Pre-1988 INPI data added to MARPAT  
NEWS 4 FEB 21     STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results  
NEWS 5 FEB 22     The IPC thesaurus added to additional patent databases on STN  
NEWS 6 FEB 22     Updates in EPFULL; IPC 8 enhancements added  
NEWS 7 FEB 27     New STN AnaVist pricing effective March 1, 2006  
NEWS 8 MAR 03     Updates in PATDPA; addition of IPC 8 data without attributes  
NEWS 9 MAR 22     EMBASE is now updated on a daily basis  
NEWS 10 APR 03    New IPC 8 fields and IPC thesaurus added to PATDPAFULL  
NEWS 11 APR 03    Bibliographic data updates resume; new IPC 8 fields and IPC thesaurus added in PCTFULL  
NEWS 12 APR 04    STN AnaVist \$500 visualization usage credit offered  
NEWS 13 APR 12    LINSPEC, learning database for INSPEC, reloaded and enhanced  
NEWS 14 APR 12    Improved structure highlighting in FQHIT and QHIT display in MARPAT  
NEWS 15 APR 12    Derwent World Patents Index to be reloaded and enhanced during second quarter; strategies may be affected  
NEWS 16 MAY 10    CA/CAplus enhanced with 1900-1906 U.S. patent records  
NEWS 17 MAY 11    KOREAPAT updates resume  
NEWS 18 MAY 19    Derwent World Patents Index to be reloaded and enhanced  
NEWS 19 MAY 30    IPC 8 Rolled-up Core codes added to CA/CAplus and USPATFULL/USPAT2  
NEWS 20 MAY 30    The F-Term thesaurus is now available in CA/CAplus  
NEWS 21 JUN 02    The first reclassification of IPC codes now complete in INPADOC

NEWS EXPRESS     FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,  
                  CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),  
                  AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.  
                  V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT  
                  <http://download.cas.org/express/v8.0-Discover/>

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NEWS LOGIN       Welcome Banner and News Items  
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FILE 'HOME' ENTERED AT 13:59:34 ON 23 JUN 2006

=> file medline  
COST IN U.S. DOLLARS  
  
FULL ESTIMATED COST

SINCE FILE ENTRY	TOTAL SESSION
0.21	0.21

FILE 'MEDLINE' ENTERED AT 14:00:01 ON 23 JUN 2006

FILE LAST UPDATED: 22 JUN 2006 (20060622/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>). See also:

<http://www.nlm.nih.gov/mesh/>  
[http://www.nlm.nih.gov/pubs/techbull/nd04/nd04\\_mesh.html](http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html)  
[http://www.nlm.nih.gov/pubs/techbull/nd05/nd05\\_med\\_data\\_changes.html](http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html)  
[http://www.nlm.nih.gov/pubs/techbull/nd05/nd05\\_2006\\_MeSH.html](http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html)

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s gdh and mutant  
1031 GDH  
54 GDHS  
1045 GDH  
(GDH OR GDHS)  
169375 MUTANT  
98956 MUTANTS  
225610 MUTANT  
(MUTANT OR MUTANTS)

```
=> s l1 and (thr or t)
      13371 THR
      153 THRS
      13439 THR
                           (THR OR THRS)
4221788 T
      103 L1 AND (THR OR T)
```

```
=> s 12 and (thr366 or t366)
      4 THR366
      3 T366
L3          0 L2 AND (THR366 OR T366)
```

=> 12 and 366

L2 IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.  
For a list of commands available to you in the current file, enter  
"HELP COMMANDS" at an arrow prompt (>).

=> s 12 and 366  
5754 366

L4

0 L2 AND 366

=> l2 and asp

L2 IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.

For a list of commands available to you in the current file, enter

"HELP COMMANDS" at an arrow prompt (=>).

=> s l2 and asp

20176 ASP

265 ASPS

20368 ASP

(ASP OR ASPS)

L5

7 L2 AND ASP

=> d ibib abs 15 1-7

L5 ANSWER 1 OF 7 MEDLINE on STN

ACCESSION NUMBER: 2005158903 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15736973

TITLE: Spontaneous chemical reversion of an active site mutation: deamidation of an asparagine residue replacing the catalytic aspartic acid of glutamate dehydrogenase.

AUTHOR: Paradisi Francesca; Dean Jonathan L E; Geoghegan Kieran F; Engel Paul C

CORPORATE SOURCE: Department of Biochemistry, Conway Institute of Biomolecular and Biomedical Research, University College Dublin, Belfield, Dublin 4, Ireland.

SOURCE: Biochemistry, (2005 Mar 8) Vol. 44, No. 9, pp. 3636-43. Journal code: 0370623. ISSN: 0006-2960.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200505

ENTRY DATE: Entered STN: 29 Mar 2005

Last Updated on STN: 10 May 2005

Entered Medline: 6 May 2005

AB A mutant (D165N) of clostridial glutamate dehydrogenase (GDH) in which the catalytic Asp is replaced by Asn surprisingly showed a residual 2% of wild-type activity when purified after expression in Escherichia coli at 37 degrees C. This low-level activity also displayed Michaelis constants for substrates that were remarkably similar to those of the wild-type enzyme. Expression at 8 degrees C gave a mutant enzyme preparation 1000 times less active than the first preparation, but progressively, over 2 weeks' incubation at 37 degrees C in sealed vials, this enzyme regained 90% of the specific activity of wild type. This suggested that the mutant might undergo spontaneous deamidation. Mass spectrometric analysis of tryptic peptides derived from D165N samples treated in various ways showed (i) that the Asn is in place in D165N GDH freshly prepared at 8 degrees C; (ii) that there is a time-dependent reversion of this Asn to Asp over the 2-week incubation period; (iii) that detectable deamidation of other Asn residues, in Asn-Gly sequences, mainly occurred in sample workup rather than during the 2-week incubation; (iv) that there is no significant deamidation of other randomly chosen Asn residues in this mutant over the same period; and (v) that when the protein is denatured before incubation, no deamidation at Asn-165 is detectable. It appears that this deamidation depends on the residual catalytic machinery of the mutated GDH active site. A literature search indicates that this finding is not unique and that Asn may not be a suitable mutational replacement in the assessment of putative catalytic Asp residues by site-directed mutagenesis.

L5 ANSWER 2 OF 7 MEDLINE on STN  
ACCESSION NUMBER: 2001306691 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11341912  
TITLE: Contribution of an aspartate residue, D114, in the active site of clostridial glutamate dehydrogenase to the enzyme's unusual pH dependence.  
AUTHOR: Coughlan S; Wang X G; Britton K L; Stillman T J; Rice D W;  
Chiaraluce R; Consalvi V; Scandurra R; Engel P C  
CORPORATE SOURCE: Department of Biochemistry and Conway Institute of Biomolecular and Biomedical Research, University College Dublin, Belfield, Ireland.  
SOURCE: Biochimica et biophysica acta, (2001 Jan 12) Vol. 1544, No. 1-2, pp. 10-7.  
Journal code: 0217513. ISSN: 0006-3002.  
PUB. COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200105  
ENTRY DATE: Entered STN: 4 Jun 2001  
Last Updated on STN: 4 Jun 2001  
Entered Medline: 31 May 2001

AB Glutamate dehydrogenase from *Clostridium symbiosum* displays unusual kinetic behaviour at high pH when compared with other members of this enzyme family. Structural and sequence comparisons with GDHs from other organisms have indicated that the Asp residue at position 114 in the clostridial enzyme may account for these differences. By replacing this residue by Asn, a mutant protein has been created with altered functional properties at high pH. This mutant protein can be efficiently overexpressed in *Escherichia coli*, and several criteria, including mobility in non-denaturing electrophoresis, circular dichroism (CD) spectra and initial crystallisation studies, suggest a folding and an assembly comparable to those of the wild-type protein. The D114N mutant enzyme shows a higher optimum pH for activity than the wild-type enzyme, and both CD data and activity measurements show that the distinctive time-dependent reversible conformational inactivation seen at high pH in the wild-type enzyme is abolished in the mutant.

L5 ANSWER 3 OF 7 MEDLINE on STN  
ACCESSION NUMBER: 2000167213 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 10702303  
TITLE: Functions of amino acid residues in the active site of *Escherichia coli* pyrroloquinoline quinone-containing quinoprotein glucose dehydrogenase.  
AUTHOR: Elias M D; Tanaka M; Izu H; Matsushita K; Adachi O; Yamada M  
CORPORATE SOURCE: Department of Biological Chemistry, Faculty of Agriculture, Yamaguchi University, Yamaguchi 753-8515, Japan.  
SOURCE: The Journal of biological chemistry, (2000 Mar 10) Vol. 275, No. 10, pp. 7321-6.  
Journal code: 2985121R. ISSN: 0021-9258.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200004  
ENTRY DATE: Entered STN: 13 Apr 2000  
Last Updated on STN: 13 Apr 2000  
Entered Medline: 3 Apr 2000

AB Several mutants of quinoprotein glucose dehydrogenase (GDH) in *Escherichia coli*, located around its cofactor pyrroloquinoline quinone (PQQ), were constructed by site-specific mutagenesis and characterized by enzymatic and kinetic analyses. Of

these, critical mutants were further characterized after purification or by different amino acid substitutions. H262A mutant showed reduced affinities both for glucose and PQQ without significant effect on glucose oxidase activity, indicating that His-262 occurs very close to PQQ and glucose, but is not the electron acceptor from PQQH<sub>2</sub>(2). W404A and W404F showed pronounced reductions of affinity for PQQ, and the latter rather than the former had equivalent glucose oxidase activity to the wild type, suggesting that Trp-404 may be a support for PQQ and important for the positioning of PQQ. D466N, D466E, and K493A showed very low glucose oxidase activities without influence on the affinity for PQQ. Judging from the enzyme activities of D466E and K493A, as well as their absorption spectra of PQQ during glucose oxidation, we conclude that Asp-466 initiates glucose oxidation reaction by abstraction of a proton from glucose and Lys-493 is involved in electron transfer from PQQH<sub>2</sub>(2).

L5 ANSWER 4 OF 7 MEDLINE on STN  
ACCESSION NUMBER: 1998371044 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 9705344  
TITLE: Mutant isolation of the Escherichia coli quinoprotein glucose dehydrogenase and analysis of crucial residues Asp-730 and His-775 for its function.  
AUTHOR: Yamada M; Inbe H; Tanaka M; Sumi K; Matsushita K; Adachi O  
CORPORATE SOURCE: Department of Biological Chemistry, Faculty of Agriculture, Yamaguchi University, Yamaguchi 753-8515, Japan..  
yamada@agr.yamaguchi-u.ac.jp  
SOURCE: The Journal of biological chemistry, (1998 Aug 21) Vol. 273, No. 34, pp. 22021-7.  
Journal code: 2985121R. ISSN: 0021-9258.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199809  
ENTRY DATE: Entered STN: 25 Sep 1998  
Last Updated on STN: 25 Sep 1998  
Entered Medline: 17 Sep 1998

AB Several mutants of quinoprotein glucose dehydrogenase (GDH) in Escherichia coli were obtained and characterized. Of these, significant mutants were further characterized by kinetic analysis after purification or by site-directed mutagenesis to introduce different amino acid substitutions. H775R and H775A showed a pronounced reduction of affinity for a prosthetic group, pyrroloquinoline quinone (PQQ), suggesting that His-775 may directly interact with PQQ. D730N and D730A showed low glucose oxidase activity without influence on the affinity for PQQ, Mg<sup>2+</sup>, or substrate, but D730R showed reduced affinity for PQQ. The spectrum of tryptophan fluorescence revealed that the local structure surrounding PQQ was not changed by D730N mutation. Based on these data, we assume that Asp-730 may occur close to PQQ and function as a proton (and also electron) donor to PQQ or acceptor from PQQH<sub>2</sub>. Substitutions of Gly-689, that are located at the end of a unique segment of GDH among homologous quinoprotein dehydrogenases, directed reduction of the affinity for PQQ or GDH activity. Therefore, the unique segment and Asp-730 may play a specific role for GDH, which might be related to the intramolecular electron transfer from PQQ to ubiquinone.

L5 ANSWER 5 OF 7 MEDLINE on STN  
ACCESSION NUMBER: 95194599 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 7888103  
TITLE: Altered GABAergic and glutamatergic transmission in audiogenic seizure-susceptible mice.  
AUTHOR: Cordero M L; Ortiz J G; Santiago G; Negron A; Moreira J A  
CORPORATE SOURCE: Department of Pharmacology, University of Puerto Rico,

CONTRACT NUMBER: School of Medicine, San Juan 00936-5067.  
2 SO6 GMO8224 (NIGMS)  
SOURCE: Molecular neurobiology, (1994 Aug-Dec) Vol. 9, No. 1-3, pp.  
253-8.  
Journal code: 8900963. ISSN: 0893-7648.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199504  
ENTRY DATE: Entered STN: 27 Apr 1995  
Last Updated on STN: 3 Feb 1997  
Entered Medline: 18 Apr 1995

AB The C57BL/10 SPS/sps mouse mutant are audiogenic seizure-susceptible. The enzymatic activities of glutamate decarboxylase (GAD), GABA aminotransferase (GABA-T), alanine aminotransferase (ALA-T), aspartate aminotransferase (ASP-T), and glutamate dehydrogenase (GDH) of whole brain supernatant are significantly reduced in these epileptic mice. GABA uptake is decreased in cortex, midbrain, and pons medulla. Previous studies showed the presence of two sodium-dependent GLU uptake systems in normal (SPS/SP) mice. Glutamate Umax by System 1 is significantly decreased in these mice, whereas the Umax value for System 2 is significantly increased in the epileptic mice.

L5 ANSWER 6 OF 7 MEDLINE on STN  
ACCESSION NUMBER: 94311821 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 8037659  
TITLE: The catalytic role of aspartate in the active site of glutamate dehydrogenase.  
AUTHOR: Dean J L; Wang X G; Teller J K; Waugh M L; Britton K L;  
Baker P J; Stillman T J; Martin S R; Rice D W; Engel P C  
CORPORATE SOURCE: Krebs Institute for Biomolecular Research, Department of  
Molecular Biology and Biotechnology, University of  
Sheffield, U.K.  
SOURCE: The Biochemical journal, (1994 Jul 1) Vol. 301 ( Pt 1), pp.  
13-6.  
Journal code: 2984726R. ISSN: 0264-6021.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199408  
ENTRY DATE: Entered STN: 25 Aug 1994  
Last Updated on STN: 25 Aug 1994  
Entered Medline: 16 Aug 1994

AB A putative catalytic aspartyl residue, Asp-165, in the active site of clostridial glutamate dehydrogenase has been replaced with serine by site-directed mutagenesis. The mutant enzyme is efficiently overexpressed in Escherichia coli as a soluble protein and can be successfully purified by the dye-ligand chromatographic procedure normally employed for the wild-type enzyme. By several criteria, including circular dichroism spectrum, sulphhydryl reactivity with Ellman's reagent, crystallization and mobility in non-denaturing electrophoresis, the enzyme appears to be correctly folded. NAD<sup>+</sup> protects the D165S mutant against modification by Ellman's reagent, suggesting unimpaired binding of coenzyme. In standard assays the specific activity is decreased 10(3)-fold in the reductive amination reaction and 10(5)-fold for oxidative deamination. Kinetic studies show that apparent Km values for NADH and 2-oxoglutarate are almost unchanged. The large reduction in the reaction rate coincides with a weakening of the affinity for ammonium ion (Km > 300 mM, compared with 60 mM for the wild-type). The data are entirely consistent with the direct involvement of D165 in catalysis rather than in the binding of coenzyme or 2-oxoglutarate.

L5 ANSWER 7 OF 7 MEDLINE on STN  
ACCESSION NUMBER: 90370274 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 2395534  
TITLE: The C57BL/10Bg sps/sps mouse: a mutant with absence-like seizures; neurochemical and behavioral correlates.  
AUTHOR: Ortiz J G; Negron A E; Garcia M T; Rosado J E; Maldonaldo C S  
CORPORATE SOURCE: Department of Pharmacology, University of Puerto Rico School of Medicine, San Juan.  
SOURCE: Neuroscience letters, (1990 Jul 3) Vol. 114, No. 2, pp. 231-6.  
JOURNAL code: 7600130. ISSN: 0304-3940.  
PUB. COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199010  
ENTRY DATE: Entered STN: 9 Nov 1990  
Last Updated on STN: 6 Feb 1998  
Entered Medline: 11 Oct 1990  
AB C57BL/10Bg sps/sps mice display behavioral arrest, similar to generalized absence seizures. Compared with the parent strain C57BL/10Bg SPS/SPS, the activities of glutamate decarboxylase (GAD, E. C. 2.6.1.15), GABA aminotransferase (GABA-T, E. C. 2.6.1.19), aspartate aminotransferase (ASP-T, E. C. 2.6.1.1), and glutamate dehydrogenase (GDH, E. C. 1.4.1.3) in whole brain crude supernatant were significantly reduced in the sps/sps mice. Alanine aminotransferase activity (ALA-T, E. C. 2.6.1.2), was not altered in any of the strains, and normalization of GAD, GABA-T and GDH activities by that of ALA-T, further revealed significant differences between the normal strain (SPS/SPS), the heterozygotes (SPS/sps), and behavioral arrest (sps/sps) mice. These results suggest the possible involvement of GABAergic and glutamatergic neurotransmission in the absence-like behavior displayed by sps/sps mice. Open field behavior of C57BL/10Bg sps/sps mice is characterized by periods of marked inactivity which easily distinguish affected homozygotes, from their heterozygotes littermates.

=> s l1 and (thr or threonine)  
13371 THR  
153 THRS  
13439 THR  
(THR OR THRS)  
45169 THREONINE  
316 THREONINES  
45313 THREONINE  
(THREONINE OR THREONINES)  
L6 1 L1 AND (THR OR THREONINE)

=> d ibib abs 16

L6 ANSWER 1 OF 1 MEDLINE on STN  
ACCESSION NUMBER: 2002714401 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 12324473  
TITLE: Substitution of Ser for Arg-443 in the regulatory domain of human housekeeping (GLUD1) glutamate dehydrogenase virtually abolishes basal activity and markedly alters the activation of the enzyme by ADP and L-leucine.  
AUTHOR: Zaganas Ioannis; Spanaki Cleanthe; Karpuras Michael; Plaitakis Andreas  
CORPORATE SOURCE: Departments of Neurology and Basic Sciences, University of

SOURCE: Crete, School of Health Sciences, Section of Medicine,  
71500 Heraklion, Crete, Greece.  
The Journal of biological chemistry, (2002 Nov 29) Vol.  
277, No. 48, pp. 46552-8. Electronic Publication:  
2002-09-24.  
Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200301  
ENTRY DATE: Entered STN: 17 Dec 2002  
Last Updated on STN: 9 Jan 2003  
Entered Medline: 8 Jan 2003

AB Human glutamate dehydrogenase (GDH) exists in GLUD1 (housekeeping) and in GLUD2-specified (brain-specific) isoforms, which differ markedly in their basal activity and allosteric regulation. To determine the structural basis of these functional differences, we mutagenized the GLUD1 GDH at four residues that differ from those of the GLUD2 isoenzyme. Functional analyses revealed that substitution of Ser for Arg-443 (but not substitution of Thr for Ser-331, Leu for Met-370, or Leu for Met-415) virtually abolished basal activity and totally abrogated the activation of the enzyme by l-leucine (1-10 mm) in the absence of other effectors. However, when ADP (0.025-0.1 mm) was present in the reaction mixture, l-leucine (0.3-6.0 mm) activated the mutant enzyme up to >2,000%. The R443S mutant was much less sensitive to ADP ( $SC(50) = 383.9 \pm 14.6$  microm) than the GLUD1 GDH ( $SC(50) = 31.7 \pm 4.2$  microm;  $p < 0.001$ ); however, at 1 mm ADP the  $V(max)$  for the mutant (136.67 micromol min(-1) mg(-1)) was comparable with that of the GLUD1 GDH (152.95 micromol min(-1) mg(-1)). Varying the composition and the pH of the reaction buffer differentially affected the mutant and the wild-type GDH. Arg-443 lies in the "antenna" structure, in a helix that undergoes major conformational changes during catalysis and is involved in intersubunit communication. Its replacement by Ser is sufficient to impair both the catalytic and the allosteric function of human GDH